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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,686	07/25/2001	GALINA MIKHAILIVNA ERKHOVA	ERKHOV-1 PCT	2044

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,686	ERKHOV	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 6-13 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 6-13 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 6 and 9 have been amended. Claims 12 and 13 have been added. Claims 6-13 are pending and under consideration.

The text of sections of Title 35 U.S. Code not found in this action can be found in a previous action.

Claims 6-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 6-12 are broadly drawn to encompass methods wherein the antiidiotypic antiembryonic antiserum was raised in animal other than the rat. The specification as originally filed describes the production of the antiidiotypic antiembryonic antiserum starting from immunization of a rat with a rat embryo from the same genetic line, followed by immunization of another rat of the same genetic line with the spleen cells from the first immunized rat. This fails to provide adequate support for the production of an antiidiotypic antiembryonic antiserum from rodents or any other animal because the immune response against a population of embryonic antigens would be different across differing species and therefore the composition of the antiidiotypic antiembryonic antiserum would not be the same for other species as for the rat. It is recognized in the art that the production of antibodies to a collection of potential epitopes is not reliable. Clark teaches that in mice some determinants are immunogenic and produce an antibody response while others are not. Therefore there is no nexus between the activated spleen cells in a rat produced by immunization of said rat with a rat embryo from the same genetic line.

Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

Claims 6-8, 12 and 13 are drawn to a method of producing an antiserum that specifically binds to antigen-stimulated lymphocytes comprising performing a first immunization by immunizing an animal with a suspension of cells from a fetus pf the same genetic line as the animal being immunized; recovering the spleen cells from said first immunized animal and separating the lymphocytes therefore to obtain a lymphocyte suspension; performing a second immunization by administering the lymphocyte suspension to animals of the same genetic line as in the first immunization, recovering the antiserum; adding cells of whole organs of said animals to said antiserum to form a suspension, and separating the supernatant to recover antiserum that specifically binds antigen-stimulated lymphocytes. Claims 9-11 are drawn to the method of diagnosing a malignant tumor, comprising contacting the antiserum of claims 6-8, 12 or 13 with a sample of tissue, blood or other physiological sample of a subject to be examined, and determining the presence of a malignant tumor by deviation of the test result from a control test.

35 U.S.C. first paragraph requires that one of skill in the art be able to make the antiidiotypic antiembryonic antiserum of the invention and use it in the claimed method without undue experimentation and with reasonable expectation of success. The antiidiotypic antiembryonic antiserum obtained from the two consecutive immunizations is a polyclonal antiserum which binds to the idiotype of the lymphocyte suspension used for the second immunization. The lymphocyte suspension would comprise a population of lymphocytes that were recognized as "non-self" by the animal in the first immunization. Because the fetal cells used for the first immunization were of the same genetic line as the animal used for the first immunization, only antigens present on the fetal cells to which the first animal was not tolerant would be expected to evoke an immune response in said first animal and be represented within the population of lymphocytes collected from the spleen of said first animal. Thus, immunization of the second animal with the lymphocyte suspension would evoke an immune response against the idiotype of the immunoglobulins expressed on the surface of the population of lymphocytes. This antiidiotypic antiembryonic antiserum would be expected to bind to antiserum evoked from the fetal antigens not recognized as "self" on the first animal, but said antiidiotypic antiserum would not be expected to bind to the "non self" fetal antigens.

Step v) of claim 6 requires that cell of "whole organs" be added to the antiidiotypic antiembryonic antiserum to form a suspension and that a supernatant should be allowed to

separate from sediment, wherein the supernatant is the final product which specifically binds to the antigen-stimulated lymphocytes. Neither the specification nor the prior art provides teachings as to what this step should accomplish, the kind of organs needed to make the suspension, or the amount of organs required to produce the antiidiotypic antiembryonic serum which would have the qualities necessary to carry out the methods of claims 9-11 with reasonable expectation of success. The antiidiotypic antiembryonic antiserum would be a polyclonal antiserum with reactivity to a population of fetal antigens. The specification has not provided teachings regarding the type of organs to be used in step v) or the amount of organs relative to the amount of the lymphocyte suspension. The specification has not provided an in vitro assay whereby one of skill in the art could determine the types of organs needed and the amount of organs relative to a lymphocyte suspension that would be necessary to produce an antiidiotypic antiserum to carry out the methods of claims 9-11 with reasonable expectation of success. The specification has not provided theoretical teachings regarding the purpose of step v), so one of skill in the art could not envisage an in vitro test to determine the types of organs needed and the amount of organs relative to a lymphocyte suspension that would be necessary to produce an antiidiotypic antiserum with the qualities necessary to carry out the methods of claims 9-11 with reasonable expectation of success. Given the lack of teachings in the specification regarding section v) of claim 6, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to make and use the antiidiotypic antiembryonic antiserum of claim 6.

Further, claim 11 requires that the diagnosis of a malignant tumor be made using the given equation wherein a value for alpha that is equal to or greater than 1.5 is obtained. The value for alpha is reliant upon the difference between the erythrocyte sedimentation rate (ESR) of a test sample and the erythrocyte sedimentation rate of a control sample (ESR). The art recognizes that the erythrocyte sedimentation rate is a function of the interaction between erythrocytes and bridging macromolecules in the suspending fluid (the abstract of Kuo et al, Biorheology, 1994, 31, pp. 77-89). The art recognizes that the level of immune complexes in the blood are correlated with the ESR (the abstract of Adamov et al, Klinicheskaya Laboratornaya Diagnostika, 1992, No. 3-4, pp. 23-25 and the abstract of Rosenthal et al, Schweizerische Medizinische Wochenschrift, 1976, vol. 106, pp. 1116-1121). Thus, the determination of a value

for alpha will be influenced by the immune complexes formed between the endogenous antitumor antibodies in a patients blood or a immunoglobulin comprising portion thereof and the antiidiotypic antiserum. The art teaches that the antibody response of a given species to an idiotypic determinant is highly heterogeneous (the abstract of Ling et al, Clinical and Experimental Immunology, 1982, Vol. 48, pp. 1-7) and that the idiotypic determinants of a given species may not represent an immunodominant idiotypic determinant in another species (abstract of Attansio et al, Molecular Immunology, 1990, Vol. 27, pp. 513-522). Thus, the endogenous antibodies in the blood of a subject with cancer must react with some portion of the rat aniidiotypic antiembryonic serum in order to provide an altered ESR rate relative to the blood or immunoglobulin comprising portion thereof taken from a normal individual. Because the antibody response of a given species to an idiotypic determinant is highly heterogeneous and because idiotypic determinants of one species do not have a nexus with idiotypic determinant of another species, it is reasonable to conclude that an antiidiotypic antiembryonic serum from a species that is not a rat will not bind to the same extend with the endogenous antibodies in a human subject. Therefore, in order to make a determination of cancer in said subject, it would be necessary to establish a new value for alpha for each type of antiidiotypic antiembryonic serum in combination with each species of patient (which would reasonable comprise canine, feline and equine patients). Thus, in the event that the rejection of the preceding paragraph is overcome with respect to section v) of claim 6, one of skill in the art would not be able to use the equation of claim 11, with the limitation that a value of alpha equal to or greater than 1.5 being indicative for the presence of a tumor for all combinations of patient species and species in which the antiidiotypic antiembryonic antiserum was made.

All other rejections and objections as set forth in the previous Office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.,
2/22/2005

Karen A. Canella

KAREN A. CANELLA PH.D
PRIMARY EXAMINER